SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Metaxx 5 mg/ml solution for injection for cattle, pigs, dogs and cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml contains:

Active substance:
Meloxicam 5 mg

Excipient:
Ethanol anhydrous (E1510) 150 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear yellow solution, free from particles.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (calves and young cattle), pigs, dogs and cats

4.2 Indications for use, specifying the target species

Cattle:
For use in acute respiratory infection with appropriate antibiotic therapy to reduce clinical signs in cattle.
For use in diarrhoea in combination with oral re-hydration therapy to reduce clinical signs in calves of over one week of age and young, non-lactating cattle.
For the relief of post-operative pain following dehorning in calves.

Pigs:
For use in non-infectious locomotor disorders to reduce the symptoms of lameness and inflammation.
For the relief of post-operative pain associated with minor soft tissue surgery such as castration.

Dogs:
Alleviation of inflammation and pain in both acute and chronic musculo-skeletal disorders. Reduction of post-operative pain and inflammation following orthopaedic and soft tissue surgery.

Cats:
Reduction of post-operative pain after ovariohysterectomy and minor soft tissue surgery.

4.3 Contraindications

Do not use in pregnant or lactating dogs or cats.
Do not use in animals suffering from impaired hepatic, cardiac or renal function and haemorrhagic
disorders, or in animals suffering from gastrointestinal disorders such as irritation and haemorrhage.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
For the treatment of diarrhoea in cattle, do not use in animals of less than one week of age.
Do not use in pigs less than 2 days old.
Do not use in cats and dogs less than 6 weeks of age nor in cats of less than 2 kg.

4.4 Special warnings for each target species

Treatment of calves with the veterinary medicinal product 20 minutes before dehorning reduces post-operative pain. The veterinary medicinal product alone will not provide adequate pain relief during the dehorning procedure. To obtain adequate pain relief during surgery co-medication with an appropriate analgesic is needed.
Treatment of piglets with the veterinary medicinal product before castration reduces post-operative pain. To obtain pain relief during surgery co-medication with an appropriate anaesthetic/sedative is needed. To obtain the best possible pain relieving effect post-surgery the veterinary medicinal product should be administered 30 minutes before surgical intervention.

4.5 Special precautions for use

Special precautions for use in animals
If adverse reactions occur, treatment should be discontinued and the advice of a veterinarian should be sought.
Avoid use in dehydrated, hypovolaemic or hypotensive animals which require parenteral rehydration, as there may be a potential risk of renal toxicity.
During anaesthesia, monitoring and fluid therapy should be considered as standard practice.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Accidental self-injection may give rise to pain. Meloxicam and other non-steroidal anti-inflammatory drugs (NSAIDs) may cause hypersensitivity (allergic reactions). People with known hypersensitivity to NSAIDs should avoid contact with the

veterinary medicinal product. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. This product may cause eye irritation. In case of contact with the eyes, immediately rinse thoroughly with water.

In view of the risk of accidental self-injection and the known adverse class-effects of NSAIDs and other prostaglandin inhibitors on pregnancy and/or embryofoetal development, this product should not be administered by pregnant women or women attempting to conceive.

4.6 Adverse reactions (frequency and seriousness)

Typical adverse reactions of NSAIDs such as loss of appetite, vomiting, diarrhoea, faecal occult blood, lethargy and renal failure have very rarely been reported from post-marketing safety experience.

Very rare cases of haemorrhagic diarrhoea, haematemesis, gastrointestinal ulceration and elevated liver enzymes have been reported from post-marketing safety experience. These side effects occur generally within the first treatment week and are in most cases transient and disappear following termination of the treatment but in very rare cases may be serious or fatal.

In cattle, only a slight transient swelling at the injection site following subcutaneous administration was observed in less than 10 % of the cattle treated in clinical studies. Anaphylactoid reactions, which may be serious (including fatal), have been observed very rarely from post-marketing safety experience and should be treated symptomatically.

If adverse reactions occur, treatment should be discontinued and the advice of a veterinarian should be
sought.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Cattle: Can be used during pregnancy.
Pigs: Can be used during pregnancy and lactation

The safety of the veterinary medicinal product has not been established during pregnancy and lactation in dogs and cats (See section 4.3).

4.8 Interaction with other medicinal products and other forms of interaction

Other NSAIDs, diuretics, anticoagulants, aminoglycoside antibiotics and substances with high protein binding may compete for binding and thus lead to toxic effects.

Do not administer concurrently with glucocorticosteroids, other non-steroidal anti-inflammatory drugs or with anticoagulant agents.
Concurrent administration of potential nephrotoxic drugs should be avoided. In animals at anaesthetic risk (e.g. aged animals) intravenous or subcutaneous fluid therapy during anaesthesia should be taken into consideration. When anaesthesia and NSAID are concomitantly administered, a risk for renal function cannot be excluded.
Pre-treatment with anti-inflammatory substances may result in additional or increased adverse effects and accordingly a treatment-free period with such veterinary medicinal products should be observed for at least 24 hours before commencement of treatment. The treatment-free period, however, should take into account the pharmacological properties of the products used previously.

4.9 Amounts to be administered and administration route

Dogs:
Musculo-skeletal disorders:
Single subcutaneous injection at a dosage of 0.2 mg meloxicam/kg body weight (i.e. 0.4 ml/10 kg body weight). A suitable oral meloxicam formulation, e.g. suspension or tablet, administered in accordance with label recommendations, may be used for continuation of treatment 24 hours after administration of the injection.

Reduction of post-operative pain (over a period of 24 hours):
Single intravenous or subcutaneous injection at a dosage of 0.2 mg meloxicam/kg body weight (i.e. 0.4 ml/10 kg body weight) before surgery, for example at the time of induction of anaesthesia.

Cats:
Reduction of post-operative pain:
Single subcutaneous injection at a dosage of 0.3 mg meloxicam/kg body weight (i.e. 0.06 ml/kg body weight) before surgery, for example at the time of induction of anaesthesia.

Cattle:
Single subcutaneous or intravenous injection at a dose of 0.5 mg meloxicam/kg body weight (i.e.10.0 ml/100 kg body weight) in combination with antibiotic therapy or with oral re-hydration therapy, as appropriate.

Pigs:
Locomotor disorders:
Single intramuscular injection at a dosage of 0.4 mg meloxicam/kg body weight (i.e. 2.0 ml/25 kg body weight). If required, a second administration of meloxicam can be given after 24 hours.

Reduction of post-operative pain:
Single intramuscular injection at a dosage of 0.4 mg meloxicam/kg body weight (i.e. 0.4 ml/5 kg body weight) before surgery.

Particular care should be taken with regard to the accuracy of dosing including the use of an appropriate dosing device and careful estimation of body weight.
Avoid introduction of contamination during use.
The stopper may not be punctured more than 50 times.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

In case of overdose symptomatic treatment should be initiated.

4.11 Withdrawal period(s)

Cattle: Meat and offal: 15 days
Pigs: Meat and offal: 5 days.
Not authorised for use in animals producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids (oxicams).
ATCvet code: QM01AC06.

5.1 Pharmacodynamic properties

Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam class which acts by inhibition of prostaglandin synthesis, thereby exerting anti-inflammatory, anti-exudative, analgesic and antipyretic properties. It reduces leukocyte infiltration into the inflamed tissue. To a minor extent it also inhibits collagen-induced thrombocyte aggregation. In vitro and in vivo studies demonstrated that meloxicam inhibits cyclooxygenase-2 (COX-2) to a greater extent than cyclooxygenase-1 (COX-1).
Meloxicam also has anti-endotoxic properties because it has been shown to inhibit production of thromboxane B_2 induced by *E. coli* endotoxin administration in calves and pigs.

5.2 Pharmacokinetic particulars

Absorption
Following subcutaneous administration, meloxicam is completely bioavailable and maximal mean plasma concentrations of 0.73 µg/ml in dogs and 1.1 µg/ml in cats were reached approximately 2.5 hours and 1.5 hours post administration, respectively.
After a single subcutaneous dose of 0.5 mg meloxicam/kg, Cmax values of 2.1 µg/ml were reached after 7.7 hours in young cattle.
Following single intramuscular doses of 0.4 mg meloxicam/kg, a Cmax value of 1.1 to 1.5 µg/ml was
reached within 1 hour in pigs.

Distribution
There is a linear relationship between the dose administered and plasma concentration observed in the therapeutic dose range in dogs and cats.

More than 97 % of meloxicam is bound to plasma proteins. The volume of distribution is 0.3 l/kg in dogs and 0.09 l/kg in cats.
The highest meloxicam concentrations are to be found in liver and kidney. Comparatively low concentrations are detectable in skeletal muscle and fat.

Metabolism
In dogs, meloxicam is predominantly found in plasma and is also a major biliary excretion product whereas urine contains only traces of the parent compound. Meloxicam is metabolised to an alcohol, an acid derivative and to several polar metabolites. All major metabolites have been shown to be pharmacologically inactive.

In cats, meloxicam is predominantly found in plasma and is also a major biliary excretion product whereas urine contains only traces of the parent compound. Five major metabolites were detected all having been shown to be pharmacologically inactive. Meloxicam is metabolised to an alcohol, an acid derivative and to several polar metabolites. As for other species investigated, the main pathway of meloxicam biotransformation in cats is oxidation.

In cattle, meloxicam is predominantly found in plasma and is also a major excretion product in milk and bile whereas urine contains only traces of the parent compound.

In pigs, meloxicam is predominantly found in plasma. Bile and urine contain only traces of the parent compound. Meloxicam is metabolised to an alcohol, an acid derivative and to several polar metabolites. All major metabolites have been shown to be pharmacologically inactive.

Elimination
In dogs, meloxicam is eliminated with a half-life of 24 hours. Approximately 75 % of the administered dose is eliminated via faeces and the remainder via urine.
In cats, meloxicam is eliminated with a half-life of 24 hours. The detection of metabolites from the parent compound in urine and faeces, but not in plasma is indicative for their rapid excretion. 21 % of the recovered dose is eliminated in urine (2 % as unchanged meloxicam, 19 % as metabolites) and 79 % in the faeces (49 % as unchanged meloxicam, 30 % as metabolites).
In young cattle, meloxicam is eliminated with a half-life of 26 hours after subcutaneous injection.
In pigs, after intramuscular administration, the mean plasma elimination half-life is approximately 2.5 hours. Approximately 50 % of the administered dose is eliminated via urine and the remainder via faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol anhydrous or ethanol 96% (E1510)
Poloxamer 188
Sodium chloride
Glycine
Hydrochloric acid (for pH adjustment)

Sodium hydroxide (for pH adjustment)
Glycofurol
Meglumine
Water for injections

6.2 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

Do not refrigerate or freeze. Protect from frost.

6.5 Nature and composition of immediate packaging

Colourless glass (type I) injection vial, closed with a
rubber stopper and sealed with an aluminium cap.
Cardboard box of 1 vial of 20 ml
Cardboard box of 1 vial of 50 ml
Cardboard box of 1 vial of 100 ml
Cardboard box of 1 vial of 250 ml
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Alfasan Nederland B.V.
Kuipersweg 9
3449 JA Woerden
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Vm 36408/3009

9. DATE OF FIRST AUTHORISATION

09 November 2022

10. DATE OF REVISION OF THE TEXT

November 2022

Approved 09 November 2022